

KRIEGER (G.)

ON THE THERAPEUTIC
VALUE OF SPERMINE,

BY
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WITH PERMISSION OF THE AUTHOR.

RECENT INVESTIGATIONS OF THE THERAPEUTIC
VALUE OF INJECTIONS OF ORGANIC FLUIDS,
ESPECIALLY SPERMINE, IN STERIL-
IZED SOLUTION.

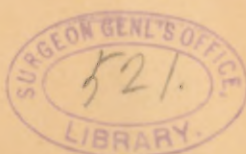
By G. E. KRIEGER, M. D., CHICAGO.

Some five years ago the eminent physiologist and neurologist, Brown-Sequard, established the fact that the testicles of young animals contain chemical substances of high dynamogenetic properties, and since then a great many scientific investigations have been made in order to reveal the character of these agents. The novelty of this discovery led, at first, to very different criticisms, and the prevailing incredulity that anything could exist which would be of such remarkable power as claimed by the author, rendered the majority of the profession unquestioning opponents of the new doctrine. The announcements of Brown-Sequard regarding injections of testicular juice on patients suffering from nervous and functionary debility, were ridiculed and frequently, without examination, Brown-Sequard's statements were flatly denied.

The efforts of the inventor of this method could not prevent that advantage was taken of the fact that some failures and septic accidents occurred, probably due to a lack of asepsis in the preparation of the remedy, or during its application, and for quite a while his method seemed to be condemned as well by the public as by the profession.

However, reports of other experimenters became more and more encouraging, and what first had been looked upon as a worthless idea of an enthusiastic head, is to-day considered a discovery of the greatest therapeutic value. In fact, the remarkable results obtained in some nervous affections, which previously were irremediable, have made the subject worthy of the most careful investigation.

In 1878 the German chemist, Phil. Schreiner, as described in the *Annals of Chemistry and Pharmacology*, found by analysis in testicular juice a substance called spermine, which, at first, by other chemists was declared identical with aethylenimin. Later, however, by the ingenious researches of Prof. Alexander Poehl, in St. Petersburg, it was proven that spermine is an organic base with characteristic properties, and that it can be prepared from



almost any organ, especially the various reproductive glands of animals.

Prof. Poehl's first publication of these investigations before the St. Petersburg Medical Society, in 1890, was received with great interest by the Russian and German profession, and was soon followed by clinical experiments of noted medical men, who all agreed that spermine is the active principle of Brown-Sequard's fluid and, as a stimulant, a therapeutic of unlimited value.

Such prominent physicians as Dr. Rotchinin and Prof. Tarchanow, in St. Petersburg, have reported a great number of cases treated successfully with spermine injections.

From these and many other experiments, Dr. Rotchinin came to the following conclusions: The effect of spermine injections is that of a strong stimulant, and corresponds with those obtained by injections of Brown-Sequard's fluid. It has, however, several advantages over the latter: 1. No danger of local inflammation, as frequently observed after the use of Brown-Sequard's fluid. 2. No fever or other symptoms caused by septic elements. 3. Equality of concentration of the fluid administered.

According to Prof. Tarchanow's investigations, a direct effect of spermine injections upon the blood's circulation has been observed. The action of the heart is greatly retarded, and the height of the pulse wave and its strength, as shown by the sphygmograph increased five times, and even more. These phenomena are explained by the stimulation of the nervous centers, especially the heart ganglia and the vasomotor nerves. Doctors Sicharew and Hubbenet, in the St. Petersburg Kalinkin Hospital, reported the following interesting case:

A woman twenty-nine years old, who suffered since thirteen years with syphilis, was treated with blue ointment for six years. She became very anemic; had at the time three ulcers on her forehead, two of which affected the bone; on the right radius periostitis gummosa, which made the movement of the hand very painful; inflammation of the right knee joint, which was greatly swollen; periostitis of the right tibia; edema of the lower limb and foot; movability of the right knee joint but fifteen degrees; gait very uncertain, digestion poor, frequent diarrhea, pulse weak. In this condition the patient was put under the treatment of spermine injections. The pulse, strength in the right hand and general feeling improved after the second injection. Pain of the right wrist decreased, edema of the leg disappeared, and even the movability of the knee was restored almost to the normal condition after five in-

jections. The pulse, 106 before, fell to 86. The digestion became normal, and the muscular strength increased about fifty per cent within ten days.

Another startling effect was obtained by Dr. Prochorow, on a man who suffered from chronic ulcers of the lower leg, and who had been treated for several months in a hospital without success. After the second injection the ulcers commenced to heal, and within three weeks the patient was cured. From these and a great many other results, published by competent authors, one is justified in concluding that spermine has doubtless some dynamogenetic power, and it remains to be explained what function it has as a normal factor of the organism.

We know that by the chemical change of material some products originate which are poisonous to the system and are, therefore, by the aid of some glandular organ, discharged from the circulation. Without doubt such poisonous products must have antagonists which render them comparatively harmless during their presence in the body, and in this way prevent auto-intoxication. Therefore such agents are of substantial importance to the system. In an average healthy organism a physiological balance is observed between these two chemical opponents. If the noxious products increase or the stimulating agents decrease, it means a lack of resistance and strength; a disposition to disease. If, on the other hand, the stimulating agents are predominating, it means vigor and health. If such be the case why should it not be possible, by the introduction of such stimulating agents into the system, with which the organism defends itself, to overcome the lack of resistance brought on by any cause detrimental to health.

The difficulty, of course, will be to prove that the substance artificially obtained is identical, or at least similar, to those prepared in the organism. It is not very long ago that Charcot and Leyden made the discovery that in certain diseases on the surface of the lungs, spleen and other organs, small crystals appeared, the significance of which was not understood until later examinations revealed their chemical composition. The crystals found especially in asthmatic persons, and known as Charcot-Leyden crystals, are nothing else but phosphate of spermine. These crystals have also been found in the discharges of persons with typhoid, consumption, cholera, in leucemia and other diseases. By their discharge from the circulation, the organism of such patients evidently lost a quantity of spermine, and therefore such stimulation to the nervous centers as would be necessary to check the power of weaken-

ing elements. The evidence of the chemical relation between these crystals and spermine led to the treatment of asthmatic persons with injections of spermine, and as anticipated, generally with good, sometimes with excellent success. Lately I treated a case which greatly improved after ten injections. There can, therefore, be no doubt that spermine has a stimulating effect upon those centers to which asthmatic attacks are attributed.

Not less remarkable results were obtained in cases of neurasthenia and anemia. Prof. Sicharew¹ reported several cases of severe neurasthenia, with agrophobia and claustrophobia, those strange phenomena in persons who become dizzy and nervous while being in a wide field, and who feel frightened when inclosed in a room, in which cases these symptoms disappeared after injections of spermine. In another case of severe anemia, in which the person had nine or ten hysteric spells daily, suffered from insomnia and great weakness, perfect cure was obtained. An old gentleman, sixty-three years of age, with general debility, apathetic to his surroundings, unable to follow a conversation, or to move about, improved so much that he could walk alone and grew stronger physically and mentally.

A special effect seemed to be obtained by spermine upon the spinal plexus; quite a number of cases of locomotor ataxia have been reported in which either a perfect and lasting cure, or at least, a great improvement was the result of spermine injections.

A patient of Dr. Sicharew², fifty-three years old, with myelitis of the lumbar part of the spinal cord, causing paresis of the lower extremities, incontinence of urine, constipation and loss of sexual energy, recovered after nine injections.

To quote from the statistics of 182 cases recently published in the *Berlin. klin. Woch.*, an exceedingly good effect was secured in fifty-two cases of neurasthenia. Only two did not show an improvement. From fourteen cases of locomotor ataxia, twelve, from twenty-three with other nervous troubles, twenty-one improved; also fifty-seven with general debility, nine with scorbutus, fourteen with consumption, have shown a favorable effect.

Very much interested by all these reports, I have made this subject a special study for over a year and have investigated the therapeutic value of spermine on my patients. To have sufficient material without depending on the Russian drug, which is very expensive, about two dollars a dose, I have experimented for four-

¹*Berl. klin. Woch.*, No. 40, 1891.

Petersburg med. Ges. February 26, 1891

teen months in my laboratory, fitted up for the purpose of securing an equally effective substance, and finally succeeded in getting the specimen I wished to obtain. I also, by the courtesy of Prof. Poehl, in St. Petersburg, with whom I communicated, obtained possession of a quantity of his preparation, which I used to compare the effects obtained from his spermine and from that prepared by myself. The result was equally favorable in cases selected for this treatment. I have since been supported in the investigation of the therapeutic value of my product by other gentlemen who are present to-night, and now take occasion to introduce to your notice several patients who have been successfully treated by spermine injections.

CASE I. Mrs. H., thirty-nine years old, five feet, three inches high, very stout, weighs 190 pounds. Has always menstruated regularly, but generally with great pain, was married sixteen years ago, has two children. For the last two years she has suffered from abdominal and lumbar neuralgia, for which she was repeatedly treated, without success. The abdominal organs are in normal condition. Patient had also frequent palpitations and neuralgic pain of the heart, was very irritable, nervous and easily frightened; could not sleep well, and complained of frequent headaches. In this condition she came to me three weeks ago. Taking the symptoms described as caused by general neurasthenia, I advised her to be treated by spermine injections. After one injection of a ten grain spermine solution she felt easier and quieted. She received one dose daily for nine days, during which she evidently improved. On the fifth day she stated that all her ailments had left her, and her husband claimed that she had changed remarkably. It is now twenty days since the first injection was given, and for the last two weeks the patient has felt perfectly well.

CASE II. This gentleman, who is seventy years old and, as you see, in apparently very good condition. He was never sick up to his sixty-fifth year; in 1889 he had an attack of inflammatory rheumatism; in 1890 was treated for gravel in the bladder, which disappeared after the use of lithia water; and for the last four years has complained of neuralgic pain in the head and lumbar region, heaviness in the legs, general weakness and insomnia. I attributed these symptoms, naturally, to his advanced age, and thought spermine would refresh him. The injections, given as usual in the back, affected him in a peculiar way. He claimed to feel them all through his chest as a warm, stimulating agent, and soon assured me of their good effect upon his general health. The neu-

ralgic pain in the back and weakness in the limbs disappeared, his sleep and strength improved, the headache became less, and he says he feels twenty-five years younger.

CASE III. Of special interest, I think, is another case which I would like to present, and about which I would be glad to hear the opinion of some gentlemen who make diseases of the nervous system a specialty. From the most apparent symptoms, I may call it a case of spinal sclerosis, but it seems to me that there are also other atrophic processes, possibly of cerebral nature. As far as I could learn, the history is as follows: The patient, a man fifty-seven years old, five feet ten inches tall, weight 230 pounds, was always in good health up till March, 1893. He did not indulge in alcoholic drinks, never suffered from syphilis, but was a heavy smoker. In March, 1893, he complained of slowly growing weakness in the right, later in the left, leg. His limbs felt as if burdened by weights. Then a constant dizziness in the head set in. He was treated for apoplexy, with no effect. The weakness in his legs progressed until they would not carry him. His dizziness also grew worse; he became irritable, nervous, could not sleep, but had fair appetite and digestion. He was under the treatment of several physicians, the last of whom, suspecting the disease was of syphilitic origin, put him under inunctions and iodide of potash. The patient lost about thirty pounds. His condition, however, did not improve, and when I saw him first, on February 6, I found the following condition:

A man, strongly built, sat in an arm chair, his features showed signs of despair, his eyes were clear but unsteady, he was unable to rise or even to raise his legs, but could move his arms pretty freely. His grasp was weak, and the movement of the hand and arm somewhat incoördinated; for instance, when he wanted to reach for something he failed to strike it. The fingers spread apart, trembled; at the tips and under the sole he had a numb and prickling sensation. He was free of pain, but complained of a heavy and dizzy feeling in his head. Pupil reflex was good. When lifted from the chair he could stand, his legs spread apart about eighteen inches. With closed legs he tumbled. He also became very uncertain with his eyes closed. Supported on either side, he tried to walk; the legs were moved with difficulty and incoördinately; the feet were swung forward and set down with force; brought back to his chair he felt very tired. The sensibility of the skin and reflex of the patella was but little disturbed. The functions of the bladder and rectum have lately become weak, the

patient has frequent inclination to pass urine, the examination of which showed nothing abnormal. Examination of the eyes showed atrophy of the left optic nerve. For the last two months he has been unable to lie down; was obliged to sit up all night, and compelled to sleep in his chair. He also complained of an almost constant ringing noise in his ears.

In this condition I subjected him to a treatment of spermine injections, with the following effect: After five injections he could easily rise and stand with his heels and toes together. He had fifteen injections altogether, and is now able to walk fairly well, even to climb stairs with some effort. He feels a great deal stronger, can lie down and sleep sometimes all night. During this treatment I avoided any other therapeutic aid. The only symptom that still annoys him is the dizziness in the head, to which he pays the more attention since being relieved from the confinement to his chair.

On these, and quite a number of other cases, I have studied the effect of spermine injections, and have had in some of them surprisingly good results, while the rest were more or less favorably affected. One feature I would like to emphasize; spermine seems to be a direct antidote against the bad effects of anesthetics, probably due to the stimulation of the heart's action. In 1891 the Russian surgeon, Weljaminoff, and recently I also have observed that patients who received one spermine injection shortly before an operation had a splendid narcosis, and no nausea or any other bad effect after they awoke.

In order to ascertain if this condition was really obtained by the action of spermine, I have experimented in the Chicago Hospital on a patient who had to take ether several times. He was a man of thirty-nine years, upon whom I was going to perform Lange's or Whitehead's operation for hemorrhoids. He received a fifteen grain spermine injection shortly before the anesthetic was given. He was one hour and a half under the influence of ether; had a splendid narcosis, and when he awoke felt perfectly well. Eight days later I gave ether to remove the stitches without using spermine. He then was only fifteen minutes under the influence of the narcotic, but it took him all day to overcome the nausea and bad feeling with which he awoke. It is, of course, a question in how many cases such a favorable effect will be obtained, and I do not doubt that frequently the injections may fail to act as desired, but still I think it may be worth trying.

Before I conclude I wish to say a few words about the chemi-

cal and physiological properties of spermine. Spermine, according to the analysis of Phil. Schreiner, *Ann. Chem. & Pharm.* 1878, p. 194, is a substance with the chemical formula, $C_2 H_5 N$. Like other bases it forms salts when in contact with acids or metals. Some of these salts are long prismatic crystals which, though prepared by chemicals, retain the physiological properties that spermine possesses. Such crystals I have photographed from microscopical specimens; the specimens were obtained from preparations from different organs: No. 1, from testicles of a young bull; No. 2, from ovaries of a young cow. Numbers 3 and 4, prepared in a different way, are not as pure as the first ones; No. 3 is made from a small quantity of genuine Brown-Sequard fluid; No. 4, from an extract of pancreas. Regarding the chemical composition, spermine belongs to the group of the imins, and has at first by some chemists been taken for aethylenimin, which has the formula $C_2 H_4 NH$; that is, the same elements, but in another group. By the investigations of Prof. Poehl this opinion has been proved to be a mistake. He found that spermine is a base per se, with certain characteristic properties different from other substances, with equal elements. Some of its reactions are: 1. With chloride of gold it forms a yellow precipitate, which later changes into flat crystals. 2. With chloride of platinum it forms a crystalline precipitate. 3. With tungstate of sodium it gives a cloudy precipitate soluble in alkalies, insoluble in acids. The most characteristic property is a smell like human sperma, if spermine is brought in contact with chloride of gold and metallic magnesium.

I have here a sample of such combinations, and you may convince yourselves that my preparation really contains spermine. It was for these reactions that I worked over a year and made many thousands of experiments; after which I learned to understand why such a noted firm as Merck & Co., pronounced in the *Pharmaceutical Zeitschrift for Russia*, in 1890, that they did not succeed in preparing this valuable substance. The same statement has been made by other chemical firms; and I think this is the reason why, up to date, spermine has not appeared in the list of our modern therapeutics. Prof. Poehl himself said, in the *Berlin. klin. Woch.*, 1891, "The conditions by which spermine crystals may be obtained from solutions which contain spermine, are sometimes very difficult to determine;" and I also have found that, when I repeated the same process on the same preparation, I would at times not obtain the same crystallization as previously found.

Regarding the physiological action of spermine, chemical and

physiological experiments have revealed the fact that the stimulation and otherwise beneficial effects from spermine injections are very natural. Since it is known that spermine is not only an important factor of the reproductive glands in the male and in the female organism, but also exists in the thyroid gland, the thymus, pancreas, spleen and other organs, it has become evident that spermine is a normal substance circulating in the blood, which has to and does accomplish a certain task in the economy of life. Medical science was greatly mistaken when it was believed that some organs, as the spleen, subrenal glands and others, were of no use in biological respects, and could just as well be parted with. By the bad effect obtained from the extirpation of the thyroid gland, we have been convinced that in this, as in other glands, a substance is produced which is absolutely necessary for our system, and which is probably similar to spermine; and so, I believe that an important function of these organs is the production of spermine. The fact that male animals deprived of their sexual glands in their early days, cannot compete in strength with their brothers who are still in possession of these vital organs, has led to the interesting experiment on dogs to inject spermine as a substitute. Of four young dogs, all brothers, two treated this way, after being castrated, grew twice as large and strong as the other two. The incorporation of such substances as are produced in our glands into the blood, is therefore a very natural support of a physiological process.

The manner in which spermine acts upon the organism has been carefully studied by Tarchanow, Poehl and others, who are of the opinion that the stimulative effect of spermine is due to its great oxidizing power. This theory is supported by the following facts:

1. Metallic magnesium in solution of the chloride of a metal changes into oxide of magnesia, by the influence of spermine already in very small quantity.

2. The blood, if influenced by chemical agents which diminish its oxidizing power, as chloroform, oxide of nitrogen, strychnia, urea, can be brought to its normal condition by the support of spermine. This explains the favorable effects of spermine injections during and after narcosis.

3. A direct test for the oxidizing power of spermine was obtained by quantitative examination of the urine before and after spermine injections, which showed a stronger oxidation of the albuminoids after the injections.

From these facts it does not seem strange that in diseases which diminish the oxidizing energy of the blood and nervous system, as in neurasthenic, anemic, cachectic persons, spermine injections have a very favorable effect. The same observation has been made in auto intoxications; that is, in diseases where the products of the regressive albumen metamorphosis accumulate in the organs.

A very important factor for the effect of spermine is the alkalinity of the blood. As a rule in all the diseases named, as well as in acute fevers, as typhoid, scarlet, pneumonia, erysipelas, the blood possesses a high degree of acidity, in which spermine becomes insoluble and therefore inactive. If the acidity is neutralized, as for instance in diabetes, by the use of Carlsbad salts, the spermine regains its activity and the improved oxidation causes the disappearance of sugar in the urine. The same result has been obtained without alkalizing the blood by artificial introduction of spermine. As the latter is a normal substance of the organism, its application is an imitation and support of nature, and therefore entirely harmless if used under certain precautions.

It is *different from Brown-Sequard's fluid*, inasmuch as the latter contains a number of substances, as kreatin, kreatinin, hypoxanthin, lecithin, guanin, nuclein, and so on, which do not benefit and may hurt. Furthermore, as it is known that the organs from which the emulsion known as Brown-Sequard's fluid is obtained, often contain the germs of disease, and as other products, the toxines, cannot be eliminated in the way the fluid is prepared, the injection of this fluid is in a strict sense of asepsis, not a safe method. The injections are sometimes followed by an abscess, an accident that has recently occurred in this city, even in the hands of a physician of very high standing, a complication I have never observed nor seen reported after spermine injections.

The isolation of the active principle is therefore of vital importance, and has besides the advantage that the dose can be regulated, which is impossible in Brown-Sequard's fluid, because no one can tell how much spermine it contains. The solution I use is equal to 2 per cent, and is always bacteriologically tested before being put in flasks, so I am sure it is aseptic; and although I do not claim that it will have the desired effect in every case, on the contrary am fully prepared to see occasionally a failure, I think the subject is worth study.

As far as the technique is concerned, I have found it advisable to use a series of from ten to fifteen injections, one a day; commencing with small doses, about 5 to 10 minims, and gradu-

ally increasing the dose to 20 minims. The number of doses required is, however, a matter of personal judgment, and sometimes two or three injections are sufficient to secure a remarkable effect.

In order to keep this solution perfectly aseptic I have put up single doses in separate flasks, like the one shown. They are opened by striking the neck, which will break at the mark. The fluid is then taken out by a hypodermic needle, which should always be thoroughly cleaned before and after using. The most aseptic instrument for the purpose is a syringe with a piston of asbestos. It seems practical to inject very slowly after the skin has been thoroughly sterilized. With these precautions I have never had any trouble, except slight local irritation.

In conclusion, I wish to recount the different effects obtained by spermine injections in various diseases treated by other physicians and myself.

1. The action of the heart is stimulated.
2. The respiration becomes easier, more regular and less frequent.
3. The general feeling improves.
4. The muscular strength increases.
5. Sleep and appetite improve.
6. Edema, due to lack of power in the arterial system, disappears.
7. Sugar in the urine decreases.
8. Ataxy of muscles, especially caused by spinal troubles, decreases.
9. Neuralgia, especially of lumbar origin, disappears.
10. The sexual functions are stimulated. This may be taken as a result of general improvement, but in my estimation, should not be considered a specific effect.
11. The functions of the bladder, kidneys and intestinal tract improve.
12. Local reactions are either of a slight and harmless nature, or do not happen at all.

Although such favorable results have been recorded in hundreds of cases, I do not wish to say that they will always be obtained, and we have to be prepared in some cases to miss the desired effect. The exceptions, however, do not speak against the method as a whole, but rather, as the Latin phrase says: "*Exceptio firmat regulam.*"

PRESENTATION OF PATIENT.

Dr. G. E. KRIEGER : In addition to the paper I read before this society a month ago on the effect of spermine injections, I wish to exhibit this patient who used to suffer from chorea.

The patient is a girl ten years of age, resident of South Chicago. Since the middle of last August, she has suffered from chorea which became so severe that she could not walk. She entirely lost control of her limbs, legs as well as arms; she could not feed herself, could not carry anything in her hands, and was a perfect invalid.

She came under the care of Dr. Ed. Bert, who advised the parents to submit her to the treatment of spermine injections. The result was that after five injections all the irritability, which was so pronounced, was gone, and she became a normal child, as you see her to-night, and has ever since been entirely well. Before the treatment she could not sleep, but was very restless, but now she sleeps as soundly as any one, eats normally, and is in every other way perfectly developed.

I have received reports from physicians as to different diseases that have been treated by spermine injections; one was a case of locomotor ataxia that improved after ten spermine injections so much that the patient could walk fairly well alone for about half a mile without fatigue.

Another patient suffering from severe neurasthenia was greatly improved after six spermine injections. A special feature I would mention is the effect of spermine in narcosis; it removes the bad effect of anesthetics, chloroform as well as ether. Spermine injections have been used quite extensively in the Chicago Hospital with uniformly good results, the patients awake after narcosis without nausea or vomiting.

In about forty-five cases spermine injections were used under my supervision, and in about ninety per cent of these cases the effect was perfect; in ten per cent it was very difficult to decide whether a mistake was made regarding the time in which the spermine injections were given, they being administered during the narcosis, instead of ten minutes before, or something else was to blame for lack of result. Spermine injections have had, so far, in a great many cases a very good stimulating effect, and I would repeat my offer to the profession that if any one wishes to make an experiment I will be glad to furnish the material.

RECORD OF CASES, TREATED WITH SPERMINE.

Published in the *St. Petersburger Med. Woch.*, 1890-1894, *Berlin Klin. Woch.*, 1891, *Deutsche Med. Woch.*, 1892, *Chicago Medical Recorder*, 1894, with some new cases added.

I. DISEASES OF THE NERVOUS SYSTEM.

Dr. SCHAFRANOFF: Neurasthenia, neuralgia of the heart. Recovery after twenty-four injections.

Dr. TULUSCHEFF: Neurasthenia and paresis of the limbs. Improvement.

Dr. BÖTHLINGK: Three cases. General debility and dizziness. Recovery after a few injections.

Dr. ROTSCHNIN: Neurasthenia, gastro-enteritis, acne. Impotenz. Recovery from all these symptoms.

Dr. SICHAREW: Thirty-two cases of neurasthenia with various complications, such as dyspepsia, anemia, debility, headache, asthma, etc. Recovery or improvement in thirty-one cases.

Dr. FINKELSTEIN: Three cases. Patient of twenty-eight with constant headache, insomnia, constipation, lack of appetite, anemia, palpitation of the heart, etc. Greatly improved after a few injections. A girl of nineteen, with similar symptoms showed likewise improvement. A woman of thirty-three, with general neurasthenia, dyspepsia, insomnia, increased irritability. When treated by injections of spermine rapidly improved.

Dr. OSTROMOFF: Neurasthenia with psychic alteration, insomnia, neuralgia of neck and back. No effect from iron, phosphate, bromides, electricity, etc. After nineteen spermine injections, lasting improvement of all symptoms.

Dr. A. F. RAMOWITSCH: Patient of thirty-five suffering from asthmatic spells, great irritability, stenocardia, palpitations of the heart, constipation, rheumatic pains, lack of appetite, etc. Recovered to perfect health after twelve injections.

Dr. NAGORSKY: Neurasthenia and dyspepsia of fifteen years' standing. No remedies had any effect. After twelve injections perfect recovery.

2. LOCOMOTOR ATAXIA.

Prof. EULENBURG: *Encyclop. Jahrb.*, p. 650. A severe case of locomotor ataxia showed considerable improvement after the injections.

Prof. JOFFRAY: Salpetriere, Paris. Three cases. The ataxia and general condition of these cases rapidly improved after five, eleven and thirteen injections respectively.

Dr. SAWITSCH: Patient of sixty-five with ataxia, paresis of sphincter ani and bladder. Recovered and gained strength after the injections.

Dr. SICHAREW: Patient of thirty-three. Since six years ataxia and debility, weakness of bladder and rectum. Good improvement. Cf. *Journal of Med. Chem. and Pharm.*, No. 3.

Dr. WIKTOROW: Patient of fifty-one. Shooting pains in both legs, paraplegia, incontinentia urinae. Improvement after three injections.

Dr. OSTROMOW: Patient of fifty-two. Same symptoms as above. Both patients showed marked improvement of the gait.

Dr. ORLIITZKY: Patient of thirty years. Ataxia since over five years. Baths and suspension of no effect. Complications, retention of urine, neuralgia of legs, no reaction of pupils, singing in ears, sexual weakness, etc. Improvement commenced after eight injections, and continued until retention of urine, neuralgia, and even atactic gait had disappeared.

OTHER DISEASES OF THE SPINAL CORD AND BRAIN.

Dr. MAXIMOWITSCH. Two cases of myelitis transversa. Marked improvement; Seven cases of hysteria. Recovery.

Dr. SICHAREW: Hysteria with insomnia, chlorosis. Recovery after two injections. Lasting effect.

Dr. NEUSBERG: Lumbago. Pain decreased after a few injections.

Dr. TULUSCHEFF. Spinal irritation with anesthesia and neuralgia. Good improvement after twelve injections.

Dr. ROTSCHININ: Three cases. No. 1. Apoplexia with paresis. Hemiplegia of left side, contraction of hand, catarrh of bladder, good improvements. No. 2. Chronic myelitis, paralysis of legs, six years' standing, greatly improved after twelve injections. No. 3. Patient of seventy. Probably thrombosis of art. fossæ. Sylvii. Paralysis of facial nerves, arm and leg of right side. Marked improvement after two injections.

Dr. KRIEGER: Patient of forty-seven. Syphilitic myelitis. Paresis of both legs, contraction and ankylosis of left elbow, suppurative catarrh of bladder, neuralgia. Good improvement.

Dr. WIKTOROW: Four cases. No. 1. Patient of fifty. Hemiplegia dextra, constipation. After thirteen injections mobility of arm and leg restored. No. 2. Patient of forty-eight. Periencephalitis, spastic gait. Great muscular weakness, constipation. Marked improvement after eight injections. No. 3. Patient of forty-eight. Myelo-meningitis. Lumbar neuralgia. No locomotion even with crutches. Improved after four injections. No. 4. Patient of forty-five. Hemiparesis following apoplexia, constipation, impotentia. Marked improvement.

Dr. OSTROMNOW: Patient of fifty-six. Hemiplegia and chronic catarrh of the lungs following apoplexia. Complete paralysis of both legs, paresis of arms, night sweats, loss of memory, insomnia. All symptoms greatly decreased after three injections. No sweats, no fever, normal defæcation, good improvement of general condition.

Dr. ULRICH: Case of sciatica completely cured by the injections.

3. SYPHILIS AND SKIN DISEASES.

Dr. C. BECK, *Chicago Med. Recorder*, April, 1894: Patient of forty-seven. Syphilis when twenty-six years old. General neurasthenia, lumbar neuralgia, insomnia. Recovery after fifteen injections.

Dr. HUBBENET: Four cases. 1. Patient of twenty-four. Brain syphilis, hemiplegia dextra, muscular weakness. Pulse, 106. After two injections, pulse 80. Mobility of leg and arm greatly improved. 2. Patient of twenty-nine. Since thirteen years, lues gummosa. Ulcers on forehead, ankylosis of the right knee, periostitis of legs. Recovery after the injections.

Dr. SICHAREFF: Patient of fifty-three. Syphilitic myelitis, incontinence of urine, constipation. Recovery after nine injections.

Dr. INJASEWSKY: Patient of twenty-eight. Brain syphilis, aphasia, ptosis, rigid expression of face, weakness of muscles. Pulse, 48-52. General improvement after eight injections.

Dr. OSTROMNOFF: Patient of fifty-three. Chronic ulcers of foot and leg, chronic inflammatory rheumatism, irritability, insomnia, etc. Quick recovery from all symptoms after three injections.

4. DIABETES.

Dr. ROTSCHININ: Four cases. 1. Patient of sixty-five. After ten injections, percentage of sugar in urine reduced from 4.7 per cent to 2 per cent. 2. Patient with 5.5 per cent sugar completely cured. Cases 3 and 4 also greatly improved. *St. Petersburg Med. Woch.*, 1890, No. 31.

5. DISEASES OF THE LUNGS AND HEART.

Dr. ROTSCHININ: 1. Phthisis pulmonum (with bacilli), hæmoptysis, palpitations. Good improvement and increase of weight after ten injections. 2. Patient of fifty-three. Vitium cordis, asthma, dyspnoea. Rapid improvement. 3. Patient of sixty. Angina pectoris. Recovery. 4. Patient of eighty-four. Pneumonia duplex. In dying condition regained consciousness after one injection and lived another forty-eight hours.

Dr. BUKOCMSKY: Chronic tuberculosis, induration of lungs, sputum contained bacilli, night sweats. All symptoms disappeared after fifteen injections.

Dr. NASTJUKOFF. Patient of fifty-eight. Hæmoptysis since three years, induration of lungs on both sides, dyspnoea. Great improvement and increase of weight.

Dr. PHILIPPS: Tuberculosis, œdema of face and legs, dyspnoea. Improved considerably.

Dr. ROSSI: Two cases of pleurisy with fever. Recovered after twelve injections.

Prof. KOSTJUVIN: Angina pectoris since eight years. No attacks after eleven injections.

Dr. CHOLODKOWSKY: Patient of sixty-six; since thirty years, catarrh of the lungs; otitis media, profuse expectoration, stenocardia. Treated several times a year by injections, each time with great benefit.

Dr. KRIEGER: Three cases. 1. Patient of sixty-three; Asthma, bronchiale, dyspnoea, insomnia, greatly improved after ten injections. 2. Patient forty-eight; asthma, stenocardia, lack of appetite, recovered. 3. Child, five years old; pneumonia, crisis on fifth day, œdema of lungs, cyanosis, severe dyspnoea. After one injection of 15 minims revival and recovery.

TYPHOID AND OTHER ACUTE FEVERS.

Dr. KLIMONTOWITSCH: Patient of nineteen; severe typhoid, paresis of legs, incontinentia urinæ et alvi. Collapse. Temperature subnormal. After one injection revival, normal temperature.

Dr. SIRHAREW: Four cases. 1. Patient of thirty-eight; scorbutus, œdema of legs, pain and partial ankylosis of knee. After nine injections disappearance of symptoms. 2. Patient of fifty-five; same as above. Recovery after five injections. 3. Patient of fifty; scorbutus with large infiltrations on limbs and feet, great weakness. After the injections rapid improvement. 4. Patient of thirty-five; inflammatory œdema of left leg; sclerosis of knee. Recovery after twelve injections.

Dr. ROTSCHININ: Case of typhoid with pneumonia; weak action of the heart. Improved quickly after a few injections.

Dr. ROSSI: Five cases of scorbutus with hæmorrhages, œdema, inflammation of knee joint, etc. Recovered after twelve to twenty injections, respectively.

Dr. GRETSCHANINOFF reports at length twelve cases of scorbutus with painful infiltrations of the legs, swelling and inflammation of joints, and periosteum and disorder of the digestive tract. Prompt improvement after the injections.

Dr. SCHAPIRO: Patient of thirty-seven; arthritis deformans of thirteen years standing. Syphilis for ten years. Neuralgia of back and shoulders, limited mobility of left elbow, irritability, weakness of memory, swelling and partial ankylosis of finger joints, etc. Improvement of general condition after the injections.

Dr. PROCHAROFF: Patient of fifty-one; arthritis since six years of age. Painful swelling of joints on hands, knees and feet. Small cystic tumors on both ears, containing xanthin and urid acid. Improvement after use of spermine.

GENERAL DEBILITY AND MARASMUS.

Dr. CHOLODKOWSKY: Marasmus senilis, chronic bronchitis. Good improvement.

Dr. WIKTOROW: Patient of sixty-nine with general debility, tired feeling in legs, great irritability. Gained strength after two injections.

Dr. BUKOEMSKY: Two cases. 1. Patient of ninety-five; long standing lumbar neuralgia, lack of appetite, partial deafness. Marked improvement after eight injections. 2. Patient of forty-three; endometritis and oophoritis; abdominal neuralgia; painful menstruation, muscular atropia, etc. Complete recovery after twelve injections.

Dr. FRETIN. Patient of sixty-three; arthritis deformans, chronic rheumatism and ankylosis of joints; insomnia, lack of appetite, great weakness. Considerable improvement after the injections.

Dr. KRIEGER. Patient of seventy; lumbar neuralgia, constant headache, lack of appetite. Recovery after nine injections.

NARCOSIS.

Dr. CHORWATH (Paris Med. Acad.): Observations in sixty-one patients operated by Dr. W. 1. Cachectic persons and drunkards stand the anesthetic better after one previous injection of spermine. 2. Complications as asphyxia, vomiting, nausea are very rare. 3. No shock after the operations.

Dr. WELJAMINOFF. Four cases of prolonged operations. 1. Fibromyoma uteri; hysterectomy after four injections; duration of operation two and one-half hours; no shock, vomiting or nausea. 2. Cancer of rectum; extirpation; in spite of great weakness, splendid narcosis. 3. Ovariectomy duplex. 4. Large struma; extirpation; in all cases no bad effects from the anesthetics.

Dr. KRIEGER: Forty-five cases. In ninety per cent ideal narcosis; no vomiting, nausea or shock. Some of these patients had violent vomiting spells after previous operations without spermine.

MORPHINISM.

Dr. RITTER: Patient of twenty-six; chronic oophoritis; morphine habit since six years; daily dose 16 grains. After five spermine injections reduced to 3 grains; after another five injections no desire for the drug.

Dr. KRIEGER: Patient of forty-seven; cystitis, myelitis syphilitica, lumbar neuralgia; daily dose three to four grains. After ten injections reduced to $\frac{1}{2}$ grain.

